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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/648,168	08/26/2003	Volker Albrecht	BJA319A	4452

7590 06/09/2005

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 06/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/648,168	ALBRECHT ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment dated 3-11-05 is acknowledged. Claims included in the prosecution are 1-3 and 5-16.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-3 and 5-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specific porphyrins derivatives, 'chlorin, bacteriochlorin and other recited in claim 1 appear to lack support in the specification as originally presented and therefore, deemed to be new matter.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-2, 5 and 9-14 rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al (6,074,666) cited in the earlier action.

Desai et al disclose liposomal compositions containing hematoporphyrin, protoporphyrin, deuteroporphyrin and other porphyrins. Dipalmitoylphosphatidylcholine is the preferred phospholipid in making the liposomes. The liposomes are either in suspension form or as a lyophilized powder and contain disaccharides or polysaccharides. The compositions further contain ascorbyl palmitate. The concentration of the porphyrins ranges from 0.1 % up to 0.5 % (abstract, col. 3, lines 43-52, col. 7, line 3 through col. 8, line 52 and claims). What is lacking in Desai is the teaching of instant porphyrins derivatives. However, since Desai et al teach the applicability of the liposomal system for porphyrins in general, it would have been obvious to one of ordinary skill in the art, with a reasonable expectation of success, to use any porphyrins in the liposomes of Desai et al.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that in contrast to Desai et al, instant compositions contain one or more monosaccharides and at least one Pegylated phospholipid. This argument is not found to be persuasive since instant rejected claims do not recite these limitations.

6. Claims 1-2, 5 and 9-14 rejected under 35 U.S.C. 103(a) as being unpatentable over Madden (5,389,378) cited in the previous action.

Madden discloses liposomal formulations containing porphyrins. The phospholipids included dipalmitoylphosphatidylcholine and the liposomes are either in a suspended form or as a lyophilized powder and contain mannitol or glucose (abstract, col. 7, line 8 through col. 9, line 62, Examples and claims). The amounts of the sugars (expressed in millimolar quantities) and the amounts of porphyrins (which are expressed in microgram quantities) as evident from the examples fall within the broad ranges claimed. What is lacking in Madden is the teaching of instant porphyrins derivatives. However, since Madden teaches the applicability of the liposomal system for porphyrins in general, it would have been obvious to one of ordinary skill in the art, with a reasonable expectation of success, to use any porphyrins in the liposomes of Madden.

7. Claims 1, 11-12 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over GB 2146525 cited in the previous action.

GB discloses liposomal formulations containing hematoporphyrin, protoporphyrin, deuteroporphyrin and other porphyrins. The liposomes contain an additional anti-cancer agent (abstract, pages 5-6 and claims). What is lacking in GB is the teaching of instant porphyrins derivatives. However, since GB teaches the applicability of the liposomal system for porphyrins in general, it would have been obvious to one of ordinary skill in the art, with a reasonable expectation of success, to use any porphyrins in the liposomes of GB.

Applicant's arguments have been fully considered, but are not found to be

persuasive. Applicant argues that in GB porphyrins are bound to the surface. This argument is not found to be persuasive since instant claims do not recite where the porphyrins are present with respect to the liposomes. Applicant's arguments with regard to lack of Pegylated phospholipids in GB, are not persuasive since as pointed out above, instant claims do not recite this lipid.

8. Claims 5-10, 12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al in view of Madden both cited and discussed above.

What is lacking in DESAI et al is the use of monosaccharides such as glucose or polyols such as mannitol. The use of these sugars would have been obvious to one of ordinary skill in the art with a reasonable expectation of success since MADDEN teaches that dehydration of the liposomes can be done with a variety of sugars including those taught by DESAI et al and monosaccharides such as glucose and polyols such as mannitol.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that Madden does not teach Pegylated phospholipids. This argument is not found to be persuasive since instant claims do not require Pegylated phospholipids. Applicant's arguments that both references reject the use of monosaccharides are not found to be persuasive since Madden teaches both disaccharides and monosaccharides, but prefers disaccharides. This does not mean Madden rejects monosaccharides. Similar is the case with Desai's teachings. Applicant has not shown any unexpected results using monosaccharides compared to disaccharides or polysaccharides.

9. Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al cited and discussed above, further in view of GB 2146525 also cited and discussed above.

What is lacking in Desai et al is the inclusion of an additional beneficial agent. The inclusion of an additional agent would have been obvious to one of ordinary skill in the art to obtain an added benefit since GB shows the encapsulation of an anti-cancer agent in the liposomes is known in the art.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant once again argues that instant composition contains monosaccharides and Pegylated phospholipids. These arguments are not found to be persuasive since instant claims do not recite these limitations.

10. Claims 2, 5-10, 12-14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over GB 2146525 also cited and discussed above, in view of MADDEN cited and discussed above.

GB as pointed out above discloses liposomal formulations containing hematoporphyrin, protoporphyrin, deuteroporphyrin and other porphyrins. The liposomes contain an additional anti-cancer agent (abstract, pages 5-6 and claims).

What are lacking in GB are the teachings of lyophilizing the liposomes in the presence of sugars or polyols. Although GB teaches the use of phosphatidylcholine, it does not specifically teach that the phosphatidylcholine be dipalmitoylphosphatidylcholine.

Madden as discussed above, discloses liposomal formulations containing

porphyrins. The phospholipids included dipalmitoylphosphatidylcholine and the liposomes are either in a suspended form or as a lyophilized powder and contain mannitol or glucose (abstract, col. 7, line 8 through col. 9, line 62, Examples and claims). The amounts of the sugars (expressed in millimolar quantities) and the amounts of porphyrins (which are expressed in microgram quantities) as evident from the examples fall within the broad ranges claimed. According to Madden, the dehydrated liposomes, dehydrated in presence of protective sugars are storage stable and can be stored for extended periods of time (col. 9, lines 31-62).

It would have been obvious to one of ordinary skill in the art to used dipalmitoylphosphatidylcholine as the specific phosphatidylcholine in the liposomes of GB with a reasonable expectation of success since Madden teaches its routine in the liposomes containing porphyrins. It would have been obvious to one of ordinary skill in the art to dehydrate (freeze-dry) the liposomes of GB in the presence of protective sugars such as glucose or mannitol since dehydrated liposomes can be are storage stable and can be stored for extended periods of time as taught by Madden.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant's arguments once again pertain to monosaccharides and Pegylated phospholipids. These have been addressed above. Applicant in addition argues that 525 teaches away from instant invention and from 378 by using the porphyrins as targeting ligand as opposed to an anti-tumor agent. These arguments are not found to be persuasive since instant claims are composition claims and not method of treatment of tumors; the motivation to include an additional agent need not be the

same as in instant invention.

11. Claims 2 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al or Madden or GB cited above, further in view of Allen (Journal of Liposome Research, vol. 2 (3), pp. 289-305 (1992).

The teachings of Desai et al, Madden and GB have been discussed above. What is lacking in Desai et al or Madden or GB is the inclusion of PEG-phospholipid.

Allen teaches that incorporation of polymers such as PEG-phospholipids into liposomes results in sterically stabilized liposomes, which have several advantages over traditional liposomes (note the entire article, abstract, pages 302-303 in particular).

The inclusion of a PEG-phospholipid in the liposomes of Desai et al or Madden or GB would have been obvious to one of ordinary skill in the art because of such inclusion provides stealth character to the liposomes which have several advantages over the traditional liposomes as taught by Allen et al.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/ S Kishore

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK